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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,495	04/15/2005	Michael J Breslin	21231YP	2691

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EXAMINER	
CHU, YONG LIANG	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 08/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/531,495	BRESLIN ET AL.	
	Examiner	Art Unit	
	Yong Chu	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-9,11-15,25,26 and 38* is/are pending in the application.

4a) Of the above claim(s) *13-15,25,26 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-9,11 and 12* is/are rejected.

7)☒ Claim(s) *4,7,8 and 12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/21/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 5, 16-24, and 27-37 are cancelled by amendment filed on 15 April 2005. There is an error on line 2, page 2 of the Remarks filed 5 June 2006, stating that only Claim 22 and 23 are cancelled. Therefore, claims 1-4, 6-9, 11-15, 25, 26, and 38 are currently pending in the instant application.

Information Disclosure Statement

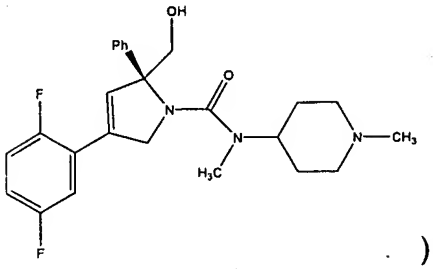
Applicant's Information Disclosure Statements, filed on 21 February 2006, have been considered. Please refer to Applicant's copies of the PTO-1449 submitted herewith.

Priority

This application is a 371 of PCT/US03/32405, filed on 14 October 2003. Applicants claim benefit of U.S. Provisional Patent Application 60/419,570 under 35 U.S.C. § 119(a-d), filed on 18 October 2002, and 60/479,712, filed on 19 June 2003.

Response to Restriction

The response to the restriction request with provisionally election of Group I (e.g. claims 1-4, 6-9, and 11-12 with election of species of the compound



) *with traverse* by Applicants' representative, David A. Muthard dated on 5 June 2006, has been considered. Applicant's arguments on pages 2-3 of the Remarks have been fully considered but they are not persuasive. Please refer to the previous Office Action.

However, rejoinder of product claims with process claims commensurate in scope with the allowed product claims will occur following a finding that the product claims are allowable. Until, such time, a restriction between product claims and process claims is deemed proper. Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution to maintain either dependency on the product claims or to otherwise include the limitations of the product claims. *Failure to do so may result in a loss of the right to rejoinder.*

The requirement is still deemed proper and is therefore made FINAL.

Status of the Claims

The scope of the invention of the elected subject matter is as follow:

As a result of Restriction Requirement, claims 13-15, 25, 26, and 38 are withdrawn from further consideration pursuant to 37 CFR 1.142 (b) as being drawn to non-elected inventions.

Therefore the subject matter which are withdrawn from consideration as being non-elected subject differ materially in structure and composition and have been restricted properly a reference which anticipated but the elected subject matter would not even render obvious the withdrawn subject matter and the fields of search are not co-extensive.

Therefore, claims 1-4, 6-9, 11, and 12 are to be examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 recites the limitation "cycloalkyl are optionally substituted.." in "R^3". However, R^3 comprises no cycloalkyl substituents. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, and 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making or using the compounds as Mitotic Kinesin inhibitor disclosed in claims 4 and 7, wherein R^3 is C1-C10 alkyl-O-Rg or C1-C10 alkyl-NRfRf', does not reasonably provide enablement for making or using the

compounds in claims 1-3, and 6 wherein R^3 is defined in claims 1-3, and 6, excluding R^3 is C1-C10 alkyl-O-Rg or C1-C10 alkyl-NRfRf'. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

For rejections under 35 U.S.C. 112, first paragraphy, the following factors must be considered (*In re Wands*, 8 USPQ2d 1400 (1988)):

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

Claims 1-3, and 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Mitotic Kinesin inhibitor of the compounds related in claims 9, and 11 does not reasonably provide enablement for each of the compound list in the claims 1-3, and 6. The claimed compounds in claim 1 for example are so structurally diversified, there are more than billions compounds have been claimed. However, as always the case for the complex 3D interaction between protein and its inhibitor, KSP protein is so specific to its binding, small structure changes to the compounds can create profound changes in biological activity. The exquisitely

stereospecific binding of ligand and receptor requires that all inhibitor (therapeutic agonists or antagonists) must be equally stereospecific. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

KSP inhibitors are used for treating cancers. There is no KSP based anticancer drug on market yet, except one on phase II clinical trial (Fraley et al. *Biorganic & Medicinal Chemistry Letters,* 2006). Therefore, the state of the art is limited to treatment of said cancer.

The level of skill in the art is high (Marcus et al. *Journal of Biological Chemistry,* 2005, 280, p11569). However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity of the closely related compounds.

Because of high level of unpredictability associated with KSP inhibitor, a greater amount of evidentiary support is needed to fully satisfy the requirement of 35 U.S.C 112, first paragraph. It is noted that pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute

predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

IDS cited reference (Fraley et al. *Biorganic & Medicinal Chemistry Letters,* 2006) discloses a pharmacokinetic profile of compound 19 in rat, dog, and monkey, using the compounds described in the specification. The compounds which are disclosed in the specification, are so narrowly defined and not closely related with most of compounds in claims 1-3, and 6.

A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that compounds fall within the scope of a claim will posses the compounds and alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724. The examples disclosed in the Specification does not enable the genus claims 1-3, and 6.

The breadth of the claims is wide, and more experimentation needed.

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which compounds would prevent for example Parkinson's disease by the method encompassed in the instant claims, with no assurance of success.

R^3 is the unique factor of the invention, and limited to C1-C10 alkyl-O-Rg or C1-C10 alkyl-NRfRf'.

Claim Objections

Claim 8 is objected to because of the following informalities: there is a typo on the first compound of page 28, wherein "1-aminium" should be "1-amine". Appropriate correction is required.

Claims 4, 7, and 12 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 6-9, 11, and 12 are provisionally rejected on the ground of nonstatutory double patenting over claims 1-10 of copending Application No.

10/559,857, 10/916,096, 10/567,676, 10/568,000, 10/915,743, 10/567,249, and 10/915,743 (junior applications). This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

Claims 1-4, 6-9, 11, and 12 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 10/517,559. Although the conflicting claims are not identical, they are not patentably distinct from each other because they claimed non-distinct compounds with same core structure.

Claims 1-4, 6-9, 11, and 12 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 10/559,857, 10/916,096, 10/567,676, 10/568,000, 10/915,743, 10/567,249, and 10/915,743 (junior applications). Although the conflicting claims are not identical, they are not patentably distinct from each other because they claimed non-distinct compounds with same core structure.

This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

Conclusion

No claims are allowed.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Chu whose telephone number is 571-272-5759. The examiner can normally be reached between 7:00 am - 3:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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